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## **MRI and ultrasonography could be useful to detect early interphalangeal osteoarthritis**

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## **Abstract**

### **Objectives:**

To assess the interest of MRI and ultrasonography (US) in identifying early and advanced interphalangeal (IP) OA.

### **Methods:**

We conducted a case–control study including patients with symptomatic hand OA (n=33) and young healthy volunteers (n=26). Proximal and distal IP joints were graded according to Kellgren and Lawrence (KL) grades. In OA patients, we separated IP joints into 2 groups: “at risk of OA” joints (potential early pre-radiographic OA joints, KL=0) and OA joints (KL=2-4). All IP joints from healthy participants were KL=0 and were considered strictly normal IP joints. Concurrently, synovitis, effusion, erosions, osteophytes, bone marrow lesions, cysts and cartilage space loss were graded by MRI and/or US. We assessed their prevalence, severity and diagnostic performance in hand OA and then compared normal IP joints from healthy participants and “at risk of OA” IP joints from OA patients as well as “at risk of OA” and OA IP joints from OA patients.

### **Results:**

The prevalence and grade of most MRI/US-detected lesions were higher in IP joints from OA patients than healthy participants. Except for osteophyte assessment, MRI seemed more sensitive than US. We found more MRI/US-detected lesions in “at risk of OA” IP joints than normal joints but also in OA than “at risk of OA” joints from OA patients. US appeared both sensitive and specific for detecting osteophytes in joints without radiographic abnormalities.

### **Conclusions:**

MRI and US give good performance for detecting radiographic and pre-radiographic OA lesions and could be interesting tools to identify early hand OA.

**Keywords:** Hand osteoarthritis; MRI; ultrasonography; X-ray; healthy individuals

## **Introduction**

The hand is the most common location for OA in the appendicular skeleton [1] with a radiographic prevalence of approximately 40% in patients over 40 years [2]. The distal interphalangeal (DIP) is the most affected joint, followed by proximal interphalangeal (PIP) [2]. Hand OA can induce severe pain and disability, thus significantly altering quality of life [3].

Hand OA is mainly diagnosed by the presence of clinical nodules and deformities and/or radiographic lesions, both reflecting an advanced stage of the disease. Indeed, X-ray abnormalities correspond to already substantial damage in the subchondral bone and cartilage. Moreover, X-rays cannot be used to assess inflammation within the synovial membrane (synovitis, intra-articular effusion) or subchondral bone [bone-marrow lesion (BML)], which play a central role in the early phases of OA pathophysiology [4,5].

MRI and ultrasonography (US) are two modern imaging techniques in the field of musculoskeletal diseases that provide a global assessment of joint tissues and can be used to assess the inflammatory part of OA with the detection of effusion and synovitis but also subchondral BML (MRI). US sensitivity is higher than X-rays for detecting osteophytes and cartilage space loss (CSL) [6,7] in addition to inflammatory features not evaluable by radiography [8]. Similarly, MRI can detect more lesions than can radiography, especially erosions and osteophytes [9–11] but also inflammatory lesions.

These imaging techniques could also be sensitive in detecting early damage in hand OA. However, an important issue in assessing the potential interest of new imaging techniques for the diagnosis of early hand OA is the lack of “gold-standard” markers sensitive enough to enable their validation. Indeed, X-rays cannot be used to detect early lesions, and so far, no biological markers have been validated for an early diagnosis of hand OA. The clinical definition of early hand OA is also difficult because it is asymptomatic in most cases. Hence, the selection of the best populations for assessing new markers for early OA diagnosis

remains challenging, especially for cross-sectional studies. One needs to include a control population for which the absence of early OA is certain and a case population for which one can reasonably consider that joints without radiographically confirmed OA are potentially the site of early OA. For this purpose, we could consider that joints from young asymptomatic individuals (< 40 years old), without OA risk factors and without radiographically detected OA lesions, are strictly “normal” joints. Conversely, joints without radiographic damage from individuals with symptomatic and radiological hand OA could be considered “at risk of OA” because they are potentially the site of early pre-radiographic OA.

According to this statement, we conducted a case–control study with the main objective being to assess the interest of MRI and US as early diagnostic tools in hand OA including two very distinct populations: 1) middle- or advanced-aged individuals with symptomatic hand OA in which the joints were separated into 2 groups: "at risk of OA" joints (potential early pre-radiographic OA joints, KL grade 0) and OA joints (KL grade 2-4) and 2) young healthy individuals without symptomatic or radiographic hand OA.

## **Methods**

### *Study design and recruitment*

We conducted a cross-sectional case–control study including patients with radiographic and symptomatic hand OA and young healthy volunteers between February 2012 and May 2013. The regional ethics committee approved this study (ID RCB: 2011-A00755-36) and all participants gave their signed informed consent.

The OA group included patients with symptomatic hand OA recruited during routine care consultations in three university rheumatology departments in France (Pitié-Salpêtrière, Lariboisière and Henri Mondor hospital). Inclusion criteria were age 30 to 85 years, diagnosis of hand OA according to American College of Rheumatology criteria [12], visual analogue scale (VAS, 0-100 mm) score for pain > 40 mm on the most painful hand at least every other day during the last month, ambulatory, frontal X-rays of hands obtained < 6 months and agreement to participate at the study after having read the written information document. Exclusion criteria were pregnant or breastfeeding, women of childbearing age without effective contraception, any history of inflammatory joint disease (rheumatoid arthritis, psoriatic arthritis, gout, chondrocalcinosis, infection, metabolic bone disease), skin psoriasis, contraindication to MRI (presence of metallic material such as a pacemaker, metallic debris in hands, surgical equipment sensitive to magnetic fields), allergy to gadolinium, severe renal impairment (Cockcroft clearance < 30 mL/min/1.73m<sup>2</sup>), history of finger fracture or surgery < 6 months, and non-affiliation to national health insurance.

Healthy participants were recruited among medical or pharmacy students, and medical and paramedical staff at Pitié-Salpêtrière hospital. Inclusion criteria were age 20 to 40 years, either sex, and absence of any clinical or radiological signs of hand OA. Exclusion criteria were any pathology affecting hands and the same criteria as for the OA group.

### Clinical assessment

Participants underwent clinical assessment at Pitié-Salpêtrière hospital during a 1-day visit. Clinical examination covered demographic data [age, sex, weight, height and body mass index (BMI)], medical and familial history, laterality of hand condition, VAS pain score, stiffness, nocturnal awakening, presence of nodes, synovitis and pain in DIPs, PIPs, metacarpophalangeal and the trapezometacarpal joint. The clinical assessor (CGV) was blinded to radiologic data.

### Radiographic assessment

Recent (< 6 months) frontal (postero-anterior) X-rays of both hands were obtained for all participants and were read by a senior trained assessor (ALT, rheumatologist) with blinding to patient identity, clinical examination and US and MRI findings. All PIPs and DIPs were graded according to Kellgren and Lawrence (KL) classification [13] taking into account osteophytes, CSL and subchondral bone sclerosis. KL grade 0 corresponds to the absence of abnormalities, 1 doubtful lesions, 2 definite osteophyte(s) with possible minimal CSL or subchondral condensation, 3 moderate osteophyte(s) with definite CSL and subchondral sclerosis, and 4 large osteophytes, marked CSL, severe sclerosis and definite bony end deformity. OA was defined as KL grade  $\geq 2$ . The presence of erosions was also noted. In young healthy participants, joints with KL grade 0 were defined as “normal” joints. In OA patients, joints with KL grade 0 were defined as “at risk of OA”. The very few joints (n = 4) classified as KL grade 1 in OA patients were excluded because they were considered doubtful OA lesions.

### US assessment

Two investigators (FG and FE, both rheumatologists) with > 10 years' experience in osteoarticular US used the Esaote Technos US machine (Genoa, Italy) for assessing hand US.

PIPs 2 to 5 and DIPs 2 to 5 were assessed from dorsal longitudinal and transversal views. The presence of B-mode and Doppler-positive synovitis, effusion, and proximal and distal osteophytes for each joint was graded from 0 to 3 (0 = absence, 1 = weak, 2 = moderate, 3 = severe) according to the US OMERACT criteria [14]. For the analysis, we used the data described above as binary variables (0 vs 1-2-3) or semi-quantitative variables (0-1-2-3). Erosions were defined as an intraarticular discontinuity of the bone surface that was visible in 2 perpendicular planes. They were assessed for each joint and considered for analysis as a binary variable (presence of at least one erosion = 1).

### MRI scoring

MRI of the most painful hand for OA patients and the dominant hand for healthy participants involved using a 0.5 Tesla (C-Scan Esaote Biomedica, Genoa, Italy) after verifying no contraindication to gadolinium injection. The following sequences were performed: axial and coronal 3D T1 +/- gadolinium and coronal STIR. All anonymized MRI images were read at a distance by two blinded experts (VF and FG, both rheumatologists), who were members of the OMERACT MRI Task Force, with consensus reached in case of any discrepancies. PIPs 2 to 5 and DIPs 2 to 5 were analyzed for presence of synovitis (T1-weighted image with gadolinium), BML (STIR images), erosion, osteophytes, bone cysts and CSL (T1-weighted image) according to a semi-quantitative grade (0 = absence, 1 = weak, 2 = moderate, 3 = severe) according to the OMERACT hand osteoarthritis MRI scoring system (HOAMRIS) [15]. Intrareader reliability was assessed in a similar MRI study of rheumatoid arthritis patients [16] and inter-reader reliability during HOAMRIS development [15]. For the analysis, we used the data described above as binary variables (0 vs 1-2-3) or as semi-quantitative variables (0-1-2-3).

### Statistical analysis



Clinical and imaging data are presented as mean (95% Confidence Interval) for continuous variables or number (%) for binary variables. To analyze similar joints for US and MRI, we used data for only PIPs 2 to 5 and DIPs 2 to 5 from the most painful hand for OA patients and from the dominant hand for healthy participants. The demographic, clinical and radiological (X-rays, MRI, US) data for each group were compared by Mann Whitney test (quantitative variables) or Chi-square test (categorical variables). The sensitivity and specificity of each US and MRI lesion were assessed from OA joint (KL grade 2-4) of OA patients and normal joints (KL grade 0) of healthy participants. Correlations between clinical data, radiographic severity and/or MRI / US features were performed with a Pearson test. Results were considered statistically significant at  $p < 0.05$ . XLSTAT (Addinsoft, Paris, France) was used for analysis.

## Results

A total of 59 individuals were included in this study: 33 with symptomatic and radiographic hand OA and 26 healthy participants. In the hand OA group, 132 PIPs and 132 DIPs from the most painful hand were studied, whereas in healthy participants, 104 PIPs and 104 DIPs from the dominant hand were evaluated. Radiographic data were available for 254 IP joints from hand OA patients (10 missing data) and for 160 from healthy participants (48 missing data).

### Comparison of demographic, clinical and X-ray data between hand OA patients and healthy participants (Table 1)

Patients with hand OA were significantly older than healthy participants (mean 65.7 vs 23.1 years;  $p < 0.001$ ) and had higher mean BMI (25.3 vs 20.7 kg/m<sup>2</sup>;  $p < 0.001$ ). Most of the hands analyzed (dominant hand for healthy participants and most painful hand for OA patients) were the right ones (88.5% for healthy participants and 66.7% for OA patients,  $p = 0.05$ ).

As expected, only OA patients presented symptoms related to hand OA (painful and swollen joints and presence of nodes), except for one healthy participant who had one painful proximal IP joint (VAS pain score = 2) without swollen joints or nodes. All PIPs and DIPs from healthy participants were classified as KL grade 0, whereas most DIPs and PIPs from OA patients were classified as KL grade 2 (47, 18.5%), grade 3 (24, 9.5%) or grade 4 (129, 50.8%) ( $p < 0.001$ ). As compared to PIPs, DIP joints from OA patients had more frequent and more severe radiographic OA (PIPs: 10.3% of KL grade 2, 10.3% of KL grade 3 and 65.1% of KL grade 4 vs. DIPs: 27.4% of KL grade 2, 8.9% of KL grade 3 and 37.9% of KL grade 4,  $p < 0.001$ ). These 200 IP joints constituted the subgroup of “OA joints”. A total of 50 (19.7%) IP joints were KL grade 0 and formed the subgroup of “at risk of OA” joints; 48.5% of hand

OA patients had thumb-base OA and 37.5% at least one erosion. No healthy participant had thumb-base OA or erosions.

#### Correlations between clinical, radiographic, MRI and US data

In hand OA patients, no correlation was found between BMI, age, and symptoms (stiffness duration, VAS pain, number of painful, swollen joints and nodes). Age was positively correlated with radiographic severity according to KL grade ( $R = 0.45$ ,  $p < 0.01$ ), but also with MRI osteophytes ( $R = 0.36$ ,  $p < 0.05$ ) and cartilage space loss ( $R = 0.37$ ,  $p < 0.05$ ). No positive correlation was found between VAS pain or BMI and MRI/US findings. Nodes were positively associated with MRI osteophytes ( $R = 0.59$ ,  $p < 0.001$ ), erosions ( $R = 0.39$ ,  $p < 0.05$ ) and CSL ( $R = 0.50$ ,  $p < 0.01$ ) and with radiographic severity according to KL score ( $R = 0.40$ ,  $p < 0.05$ ) (data not shown). In the whole population, MRI features were all significantly correlated with each other while US B-mode synovitis was correlated with Doppler synovitis and osteophytes. Most MRI and US features were also positively correlated (*Table S1*) [See the supplementary material associated with this article online].

#### Comparison of US- and MRI-detected lesions between hand OA patients and healthy volunteers (Table 2; Table S2)

On US, patients with hand OA more frequently presented B-mode synovitis, Doppler-positive synovitis and osteophytes than healthy participants. The severity of all lesions assessed by a semi-quantitative score was statistically higher in OA patients. On MRI, all lesions were significantly more frequent and more severe in OA patients than healthy participants.

Comparative analysis of PIP and DIP joints showed more effusions by US (47.2% vs. 23.4%,  $P < 0.001$ ) and more synovitis (92.7% vs. 46.0%,  $p < 0.001$ ) and BML (31.1% vs. 20.5%;  $p < 0.05$ ) by MRI in PIPs from OA patients. Similarly, there were more US effusions (46.2% vs. 20.2%,  $P < 0.001$ ), and more MRI synovitis (34.6% vs. 8.7%,  $p < 0.001$ ), erosions

(23.1% vs. 9.6%,  $p<0.01$ ), CSL (23.1% vs. 11.5%;  $p<0.05$ ) and osteophytes (27.9% vs. 16.3%;  $p<0.05$ ) in PIPs from healthy subjects. In contrast, there were more US osteophytes in DIPs from OA patients (92.5% vs. 70.1%,  $p<0.001$ ) and healthy subjects (10.6% vs. 2.9%,  $p<0.05$ ) (data not shown).

#### Diagnostic performance of US- and MRI-detected lesions for hand OA (Table 3)

OA joints (KL grade  $\geq 2$ ) from OA patients were considered “cases” and normal joints (KL grade 0) from healthy participants “controls”. Globally, the sensitivity of MRI seemed better than US for detecting hand OA lesions except for osteophytes. Indeed, osteophytes were demonstrated in 90.9% of OA IP joints by US but only 81.5% by MRI. The specificity of MRI and US features was good or excellent. Nevertheless, the specificity seemed overall better for US than MRI, especially for synovitis and osteophytes.

#### Comparison of US- and MRI-detected lesions between “normal” joints from healthy participants and “at risk of OA” joints (KL grade 0) from OA patients (Figure 1; Table 4; Table S3)

US revealed significantly more B-mode synovitis and osteophytes in “at risk of OA” than “normal” joints (synovitis,  $p<0.01$  and osteophytes,  $p<0.001$ ). The sensitivity of US to detect “at risk of OA” joints was 8.1% for B-mode synovitis, 0.0% for Doppler synovitis, 32.4% for effusions, 0.0% for erosions and 51.4% for osteophytes. Moreover, the grades of osteophytes were significantly higher in “at risk of OA” than “normal” joints (grade 1: 13.5% vs 5.6%; grade 2: 17.8% vs 1.2%, grade  $\geq 3$ : 16.2% vs 0.0%;  $p<0.001$ ). The groups did not differ in Doppler-positive synovitis, effusions or erosions.

MRI revealed a significantly higher prevalence of synovitis ( $p<0.001$ ), erosions ( $p<0.001$ ), osteophytes ( $p<0.001$ ), BML ( $p<0.01$ ), bone cysts ( $p<0.01$ ) and CSL ( $p<0.01$ ) in “at risk of OA” than “normal” joints. The sensitivity of MRI to detect “at risk of OA” joints

was 70.0% for synovitis, 42.0% for erosions, 46.0% for osteophytes, 6.0% for BML, 8.0% for bone cysts and 34.0% for CSL. Semiquantitative scoring revealed that the grade of MRI lesions was higher in “at risk of OA” than “normal” joints.

Comparison of US- and MRI-detected lesions between “at risk of OA” joints (KL grade 0) and OA joints (KL grade 2-4) in hand OA patients (Table 5; Table S4)

In OA patients, US revealed significantly more B-mode synovitis and osteophytes in OA than “at risk of OA” joints (synovitis,  $p < 0.05$  and osteophytes,  $p < 0.001$ ). OA and “at risk of OA” joints did not differ in Doppler-positive synovitis, effusions and erosions. According to the semiquantitative scoring, osteophytes were more severe in OA than “at risk of OA” joints ( $p < 0.001$ ).

MRI revealed a significantly higher prevalence of erosions ( $p < 0.001$ ), osteophytes ( $p < 0.0001$ ), BML ( $p < 0.001$ ), bone cysts ( $p < 0.001$ ) and CSL ( $p < 0.001$ ) in OA than “at risk of OA” joints. Semiquantitative scoring revealed that all MRI lesions except synovitis were statistically more severe in OA than “at risk of OA” joints. “At risk of OA” joints did not exhibit grade 3 erosions, osteophytes, BML or bone cysts, but 14.0% (7/50) exhibited grade 3 synovitis and 2.0% (1/50) grade 3 CSL.

## **Discussion**

Our study is the first to analyze in parallel radiographic, MRI, and US data in patients with advanced hand OA and young healthy participants. Given the use of data per IP joint (PIPs and DIPs), we could distinguish two types of joints without radiographic OA: those from healthy participants, corresponding to strictly normal joints, and those from OA patients, which could be considered “at risk of OA” joints as potentially the localization of early pre-radiographic OA. Thus, we compared three types of IP joints: “normal” joints from healthy participants, “at risk of OA” joints from hand OA patients and OA joints (joints with radiographic evidence of OA) from OA patients.

This original design allowed for counteracting several issues in studies assessing the potential of new diagnostic techniques in OA. The first is related to the complex identification of early OA given the high frequency of the asymptomatic form and the poor sensitivity of radiography considered the “gold standard”. Another classical issue is the usual adjustment for age in cross-sectional “case–control” studies, which favors the presence of undiagnosed early OA joints without definite radiographic damage in the “control” population, thus leading to consider the lesions detected by MRI or US on these same joints as false positives, but these could reflect early OA lesions.

We showed that MRI and US features had heterogeneous sensitivity for the diagnosis of hand OA, with osteophytes constituting the most frequent lesions. Overall, MRI seemed to provide better sensitivity, especially for synovitis in detecting hand OA, but also potential pre-radiographic lesions. Only the search for osteophytes seemed more effective with US. Although the specificity of MRI and US features was globally good, US seemed overall better, especially for synovitis and osteophytes. Indeed, MRI revealed a high frequency of synovitis (21.6%), osteophytes (22.1%), cartilage space loss (17.3%) and erosions (16.3%) in normal joints from healthy participants. However, the analysis of semi-quantitative data showed that most lesions in healthy participants were grade 1. A plausible

hypothesis for this finding could be excess sensitivity of the low-grade abnormalities causing false-positive results. This observation raises the question of the specificity of the low-grade damage and justifies caution in their interpretation. In US, only the specificity of effusions was poor (69.4%). Indeed, this feature was found in 30.6% of normal joints from healthy participants, with no statistical difference from OA joints (37.0%) even if its severity was higher in OA patients.

Higher prevalence of several MRI/US lesions in PIPs as compared to DIPs, which are the most affected by radiographic OA, may reflect a greater difficulty in analyzing DIPs and confirm poor specificity of some features such as US effusion and MRI synovitis. Conversely, the finding of more US osteophytes in DIPs supports the interest of their assessment for detection of hand OA.

Considering only joints without radiographically detected OA (KL grade 0) from the two populations, MRI revealed significantly more synovitis, erosions, BML, CSL, and bone cysts in OA patients than healthy participants. The grade of these lesions was also higher in “at risk of OA” joints from OA patients than healthy participants. These data confirm that MRI lesions, especially those with higher grades (2 and 3), could be the hallmark of early OA. US seemed less effective overall in distinguishing “normal” joints from healthy participants and “at risk of OA” joints from OA patients, particularly for synovitis and erosions. Only osteophytes seemed to be found at least as frequently with US as compared to MRI in the OA population (51.4% vs. 46.0%), with a slightly higher specificity because only 6.9% of the joints from healthy participants (5.6% of grade 1 and 1.2% of grade 2) were the site of an osteophyte according to US as compared with 20.0% with MRI (18.8% of grade 1 and 1.3% of grade 2).

Also, when we directly compared OA joints (KL grade 2-4) and “at risk of OA” joints from OA patients, MRI seemed to perform better than US. Indeed, we observed significantly more abnormalities of greater severity in OA than “at risk of OA” joints, except

for synovitis. On US, only synovitis and osteophytes were more frequent in OA than “at risk of OA” joints. When the grade of the lesions was considered, OA and “at risk of OA” joints differed only in osteophytes.

All these data highlight the great interest of osteophyte assessment, especially by US. This is corroborated by a previous study showing the detection of osteophytes by US as a useful tool for diagnosing pre-radiographic forms of hand OA [7]. Indeed, the authors detected osteophytes at inclusion in 53.2% and 21.7% of DIPs and PIPs from hand OA patients without radiographic evidence of OA, which is not much different from our study (51.4%) and showed that their presence predicted the radiographic-detected lesions. Another study assessing MRI in hand OA also showed the presence of osteophytes in almost 50% of asymptomatic IP joints [17]. However, our results suggest that osteophytes detection by MRI would be less specific as compared to US (6.9% of normal IPs from healthy subjects by US vs. 20.0% by MRI). Thus, US might be an interesting tool for the diagnosis of early OA forms by detecting osteophytes. Moreover, previous studies showed that US was a reliable exam both within and between observers [18]. For other primary lesions, MRI seems the best tool for detecting early OA.

Our work has several strengths: First, it is the first study to include an analysis per joint in both OA and healthy participants based on recent X-rays as well as MRI and US performed the same day. Second, the comparison of three different types of joints (normal, “at risk of OA” and OA IP joints) allowed for partially compensating for the lack of a reference diagnostic tool to confirm early OA damage. Finally, the use of both qualitative and semi-quantitative analyses for each lesion reinforces the relevance of MRI- and US-detected lesions as early markers of OA.

We also acknowledge some weaknesses. The first is related to the small number of enrolled participants, which limits the power of the analysis even if this is partly counterbalanced by the separate analysis of each DIP and PIP. Furthermore, this was a cross-



sectional study. The extrapolation of the status of KL grade 0 joints from OA patients as “at risk of OA” is debatable because we cannot confirm this given the cross-sectional design of the study. Only longitudinal studies with long-term radiographic follow-up would allow for confirming that these “at risk of OA” joints effectively evolve towards radiographic OA. Similarly, we cannot exclude that MRI and US lesions in “at risk of OA” joints would be related to aging rather than OA. Indeed, there is no specific data about the age-related imaging features. However, previous longitudinal studies have already shown that some MRI or US lesions such as synovitis, BML and osteophytes at baseline could predict the occurrence or progression of hand over long term which constitutes a positive argument for considering these imaging features as a marker of early OA rather than normal aging [7,19–21]. Finally, we cannot exclude an evaluation bias. Indeed, we could not maintain blinding for the investigator during the US exam requiring the presence of the participant whose characteristics were very different between the healthy and OA populations (in particular by age). Similarly, even if we ignore the group to which the patient belonged, the presence of severe damage to several neighbouring joints on MRI guided the diagnosis of hand OA and eliminated the blinding. No inter/intra-reader reliability was assessed for US and MRI in this work. However, such reliability was evaluated in previous studies [15,16] and consensus was sought between both readers in case of discrepancies in MRI evaluation.

In all, our case–control study based on an original design including two different control groups (normal IP joints from healthy participants and “at risk of OA” IP joints from hand OA patients) demonstrates an increasing prevalence and severity of most US- and MRI-detected lesions associated with radiographic severity, which reinforces the potential of these tools in the diagnosis of hand OA. It also confirms the interest of US and MRI to reveal damage in joints without radiographic abnormalities and thus diagnose early OA. However, the main result of our study is the highlighting of the great interest of US osteophytes assessment for early and late hand OA. Indeed, it provided good performance on both PIPs

and DIPs, with a better specificity and sensitivity than MRI to identify “at risk of OA” and OA joints. Osteophyte assessment by US could so be a rapid, inexpensive, risk-free and reliable way to confirm early OA. Whether the current relevance of diagnosing hand OA at early pre-radiographic stage is questionable because mostly asymptomatic and without preventive treatment, we may suppose that specific drugs would be developed in the future to limit the structural progression or development of OA, requiring early diagnosis. On the other hand, some patients may suffer from arthralgias compatible with hand OA but without X-ray lesions making the diagnosis of OA complex. Consequently, the validation of an early, sensitive, and easily performed diagnostic test such as the assessment of osteophytes by US will also be of interest in current clinical practice.

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## **Contributorship statement**

Florent Eymard and Cédric Chemla analyzed and interpreted the data. They wrote the manuscript.

Violaine Foltz, Frédérique Gandjbakhch, Fabien Etchepare and Anne-Laurence Tomi analyzed the US, MRI and/or radiographic data. They participated substantially in the review of the manuscript before submission.

Bruno Fautrel and Pascal Richette contributed to the design of the study and the analysis and interpretation of data. They participated substantially in the review of the manuscript before submission.

Cécile Gaujoux-Viala and Xavier Chevalier designed the study and analyzed, and interpreted the data. They participated substantially in the review of the manuscript before submission.

All authors approved the version submitted.

## **Competing interests**

Florent Eymard, Violaine Foltz, Cédric Chemla, Frédérique Gandjbakhch, Bruno Fautrel,

Pascal Richette, Anne-Laurence Tomi, Cécile Gaujoux-Viala have no competing interests.

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**Figure 1: MRI and ultrasound features in an “at risk of OA” proximal interphalangeal (PIP) joint from an OA patient**

*A. Coronal view of the PIP 2, an “at risk of OA” joint (Kellgren and Lawrence grade = 0). B. Coronal T1-weighted image without gadolinium, presence of a proximal lateral osteophyte (grade 1) on PIP 2 (white arrow). C and D. Axial T1-weighted image before (C) and after (D) injection of gadolinium, presence of a synovitis of PIP 2 (grade 3) (black asterisk). E. Longitudinal view of the PIP 2 by B-mode US, presence of a proximal osteophyte (grade 1) (white arrowhead).*

**Table 1. Demographic, clinical and radiographical data for healthy volunteers and patients with osteoarthritis (OA)**

	<b>Healthy volunteers (n = 26)</b>	<b>OA patients (n = 33)</b>
<b>Sex (women) (%)</b>	76.9	87.9
<b>Age (years), mean [95% CI] ‡</b>	23.1 [17.3-28.9]	65.7 [51.4-80.0]
<b>Hand considered for analysis (right) (%)</b>	88.5	66.7
<b>BMI, kg/m<sup>2</sup>, mean [95% CI] ‡</b>	20.7 [16.9-24.5]	25.3 [17.5-33.0]
<b>Pain VAS (/100), mean [95% CI] ‡</b>	0.1 [0.0-0.8]	55.2 [27.3-83.04]
<b>Painful joints (n), mean [95% CI] ‡</b>	0.0 [0.00-0.4]	2.7 [0.0-6.0]
<b>Swollen joints (n), mean [95% CI] ‡</b>	0.0 [0.0-0.0]	0.8 [0.0-2.6]
<b>Nodes (n), mean [95% CI] ‡</b>	0.0 [0.0-0.0]	4.5 [0.8-8.3]
<b>Thumb-base OA, n (%)‡</b>	0 (0.0)	16 (48.5)
<b>Erosive OA, n (%)†</b>	0 (0.0)	12 (37.5)
	PIPs and DIPs 2-5 (n=160) §	PIPs and DIPs 2-5 (n=254) §
<b>Kellgren and Lawrence grade, n (%) ‡</b>		
<b>0</b>	160 (100)	50 (19.7)
<b>1</b>	0 (0.0)	4 (1.6)
<b>2</b>	0 (0.0)	47 (18.5)
<b>3</b>	0 (0.0)	24 (9.4)
<b>4</b>	0 (0.0)	129 (50.8)

† $P < 0.01$ , ‡ $P < 0.001$ : comparisons between healthy volunteers and OA patients (Chi-square test)

§ Data were missing for 48 IP joints for healthy volunteers and for 10 IP joints for hand OA patients

95% CI: 95% confidence interval; BMI: body mass index; IP: interphalangeal; PIPs: proximal interphalangeal; DIPs: distal interphalangeal; VAS: visual analog scale



1 **Table 2. Prevalence of ultrasonography (US) and MRI lesions in PIPs and DIPs of healthy volunteers and OA patients: qualitative data**

	US		MRI	
	Healthy volunteers	OA patients	Healthy volunteers	OA patients
<b>Synovitis (US B-mode or MRI), n/tot (%)</b>	2/208 (1.0) ‡	48/215 (22.3) ‡	45/208 (21.6) ‡	172/248 (69.4) ‡
<b>Synovitis (US PD), n/tot (%)</b>	2/208 (1.0) *	11/215 (5.1) *	NA	NA
<b>Effusions, n/tot (%)</b>	69/208 (33.2)	76/215 (35.3)	NA	NA
<b>Erosions, n/tot (%)</b>	3/208 (1.4)	6/209 (2.9)	34/208 (16.3) ‡	195/264 (73.9) ‡
<b>Osteophytes, n/tot (%)</b>	14/208 (6.7) ‡	174/214 (81.3) ‡	46/208 (22.1) ‡	196/264 (74.2) ‡
<b>BML, n/tot (%)</b>	NA	NA	1/208 (0.5) ‡	68/264 (25.8) ‡
<b>Bone cysts, n/tot (%)</b>	NA	NA	3/207 (1.4) ‡	93/264 (35.2) ‡
<b>CSL, n/tot (%)</b>	NA	NA	36/208 (17.3) ‡	195/264 (73.9) ‡

2 \* $P < 0.05$ , ‡ $P < 0.001$ : comparisons between healthy volunteers and OA patients (Chi-square test)

3 *Missing data for healthy volunteers: US assessment: no missing data. MRI assessment: bone cyst = 1 IP joint.*

4 *Missing data for patients: US assessment: synovitis and effusions = 49 IP joints; erosions = 55 IP joints and osteophytes = 50 IP joints. MRI*  
 5 *assessment: synovitis = 16 IP joints.*

6 *BML: Bone marrow lesion; CSL: cartilage space loss; IP: interphalangeal; NA: not available. PD: power Doppler*

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10 **Table 3. Diagnostic performance of US- and MRI-detected lesions in PIPs and DIPs in hand OA**

	US		MRI	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
<b>Synovitis (US B-mode or MRI)</b>	24.8	99.4	68.6	78.8
<b>Synovitis (US PD)</b>	6.0	99.4	NA	NA
<b>Effusions</b>	37.0	69.4	NA	NA
<b>Erosions</b>	3.7	98.1	82.0	85.6
<b>Osteophytes</b>	90.9	93.1	81.5	80.0
<b>BML</b>	NA	NA	30.5	100.0
<b>Bone cysts</b>	NA	NA	42.0	99.4
<b>CSL</b>	NA	NA	84.5	83.1

11 *BML: Bone marrow lesion; CSL: cartilage space loss; NA: not available. PD: power Doppler*

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13 **Table 4. Prevalence of US- and MRI-detected abnormalities in PIPs and DIPs between “normal” joints (KL grade 0) from healthy**  
 14 **volunteers and “at risk of OA” joints (KL grade 0) from OA populations: qualitative data**

	US		MRI	
	“normal” joints	“at risk of OA” joints	“normal” joints	“at risk of OA” joints
<b>Synovitis, n/tot (%)</b>	1/160 (0.6) †	3/37 (8.1) †	34/160 (21.3) ‡	35/50 (70.0) ‡
<b>Synovitis DP, n/tot (%)</b>	1/160 (0.6)	0/37 (0.0)	NA	NA
<b>Effusions, n/tot (%)</b>	49/160 (30.6)	12/37 (32.4)	NA	NA
<b>Erosions, n/tot (%)</b>	3/160 (1.9)	0/34 (0.0)	23/160 (14.4) ‡	21/50 (42.0) ‡
<b>Osteophytes, n/tot (%)</b>	11/160 (6.9) ‡	19/37 (51.4) ‡	32/160 (20.0) ‡	23/50 (46.0) ‡
<b>BML, n/tot (%)</b>	NA	NA	0/160 (0.0) †	3/50 (6.0) †
<b>Bone cysts, n/tot (%)</b>	NA	NA	1/159 (0.6) †	4/50 (8.0) †
<b>CSL, n/tot (%)</b>	NA	NA	27/160 (16.9) †	17/50 (34.0) †

15 † $P < 0.01$ , ‡ $P < 0.001$ : comparisons between “normal” joints and “at risk of OA” joints (Chi-square test)

16 Missing data for “normal joints”: US assessment: no missing data. MRI assessment: bone cysts = 1 IP joint.

17 Missing data for “at risk of OA joints”: US assessment: synovitis B-mode, synovitis DP, effusions and osteophytes = 13 IP joints; erosions = 16 IP  
 18 joints. MRI assessment: no missing data.

19 BML: Bone marrow lesion; CSL: cartilage space loss; IP: interphalangeal; NA: not available. PD: power Doppler

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22 **Table 5. Prevalence of US- and MRI-detected lesions in PIPs and DIPs in “at risk of OA” joints (KL grade 0) and OA joints (KL grade 2-4)**  
 23 **from hand OA patients: qualitative data**

	US		MRI	
	“at risk of OA” joints	OA joints	“at risk of OA” joints	OA joints
<b>Synovitis (US B-mode or MRI), n/tot (%)</b>	3/37 (8.1) *	41/165 (24.8) *	35/50 (70.0)	127/185 (68.6)
<b>Synovitis (US DP), n/tot (%)</b>	0/37 (0.0)	10/165 (6.0)	NA	NA
<b>Effusions, n/tot (%)</b>	12/37 (32.4)	61/165 (37.0)	NA	NA
<b>Erosions, n/tot (%)</b>	0/34 (0.0)	6/162 (3.7)	21/50 (42.0) ‡	164/200 (82.0) ‡
<b>Osteophytes, n/tot (%)</b>	19/37 (51.4) ‡	150/165 (90.9) ‡	23/50 (46.0) ‡	163/200 (81.5) ‡
<b>BML, n/tot (%)</b>	NA	NA	3/50 (6.0) ‡	61/200 (30.5) ‡
<b>Bone cysts, n/tot (%)</b>	NA	NA	4/50 (8.0) ‡	84/200 (42.0) ‡
<b>CSL, n/tot (%)</b>	NA	NA	17/50 (34.0) ‡	169/200 (84.5) ‡

24 \* $P < 0.05$ , † $P < 0.01$ , ‡ $P < 0.001$ : comparisons between “at risk of OA” joints and OA joints (Chi-square test)

25 Missing data for “at risk of OA joints”: US assessment: synovitis B-mode, synovitis DP, effusions and osteophytes = 13 IP joints; erosions = 16 IP  
 26 joints. MRI assessment: no missing data.

27 Missing data for “OA joints”: US assessment: synovitis B-mode = 35 IP joints; synovitis DP, effusions and osteophytes = 34 IP joints; erosions = 38  
 28 IP joints. MRI assessment: synovitis = 15 IP joints.

29 BML: Bone marrow lesion; CSL: cartilage space loss; IP: interphalangeal; NA: not available. PD: power Doppler

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